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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/613,788 | 07/03/2003 | George B. McDonald | 8105-009-US-CON | 6992 |

32301 7590 04/23/2007
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| EXAMINER | |
|---|---|
| OLSON, ERIC | |
| ART UNIT | PAPER NUMBER |
| 1623 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 04/23/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/613,788 | MCDONALD, GEORGE B. | |
| | Examiner | Art Unit | |
| | Eric S. Olson | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *27 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *February 27, 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**Detailed Action**

This office action is a response to applicant's communication submitted February 27, 2007 and March 23, 2007 wherein a declaration is introduced in support of Applicant's arguments. This application is a continuation of US patent application 09/753814, now abandoned, filed January 3, 2001, which claims priority to provisional application 60233194, filed September 15, 2000.

Claims 1-18 are pending in this application.

Claims 1-18 as amended are examined on the merits herein.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's declaration under 37 CFR 1.132, submitted March 3, 2007, with respect to the various rejections of instant claims 1-18 under 35 USC 103 of record in the previous office action, has been fully considered but is moot in view of the new grounds of rejection presented below.

All rejections made in the previous office action under 35 USC 103 are withdrawn. The following new grounds of rejection are introduced:

**Claim Rejections – 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-10 and 12-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over McDonald et. al. (Reference of record in previous office action) in view of Bertz et al. (Reference included with PTO-892)

McDonald et. al. teaches that oral administration of the particular topically active corticosteroid, beclomethasone dipropionate (BDP), **alone** in the form of a capsule or **in combination with prednisone** (in the language of instant claim 16) is useful in a method of treating graft-versus-host disease in a human following organ allograft transplantation or stem cell transplantation for 30 days (see abstract and page 28, 1st paragraph, right column). McDonald et. al. also teaches that the subject has damaged tissue in the intestinal mucosa and liver, in the language of claims 3, 4, and 6 (p. 32, table 4). McDonald et. al. also teaches the effective amount of beclomethasone dipropionate to be administered as 8 mg per day (p. 29, left column, under the heading *Formulation of BDP and Placebo Capsules*), within the range of 4-12 mg/day set by the instant claim 2. McDonald et. al. also discloses that the capsules administered were either uncoated (to dissolve in the stomach) or enteric-coated (to dissolve in the intestine) in the language of instant claim 10(p. 29, left column, under the heading *Formulation of BDP and Placebo Capsules*). McDonald discloses that the treatment

was well-tolerated, and that typical side effects of corticosteroids, such as microbial infections, hypercortisolism, and adrenal insufficiency, were not observed during the treatment. (p. 32, left column, first paragraph, under the heading, "Toxicity from Treatment," and p. 33, left column, last paragraph – right column, first paragraph) McDonald et. al. also reveal the aim for the study therein to compare the effectiveness of oral BDP to that of placebo capsules in the claimed method herein, and also to examine the frequency of infection in patients treated with beclomethasone dipropionate. See abstract and the entire article, especially p. 29, left column, first paragraph and right column, 3rd paragraph. The prior art does not expressly disclose the long-term therapy (i.e., 29-56 days) in the claimed method.

Bertz et al. discloses a method of treating graft-versus-host disease by administering oral budesonide as a topically active corticosteroid. (p. 1186, left column, second paragraph - right column, third paragraph) The duration of the therapy was between 6-70 days, varying from patient to patient, with no side effects observed in any patient. (p. 1187, right column, first paragraph)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to orally administer BDP or Budesonide alone or with prednisone over the long term (i.e. 29-56 days). One having ordinary skill in the art at the time of the invention would have been motivated to orally administer BDP or Budesonide alone or with prednisone in the long term (i.e. 29-56 days) since the administration of BDP alone or with prednisone for 30 days or less is known according to the prior art, and a subject may not have fully recovered from their condition after 30 days, and further

because Bertz et al. discloses that budesonide can also be administered for the treatment of graft-versus-host disease. Thus, one of ordinary skill in the art would reasonably extend the therapy to the longer period from 30 days or less to 56 days if such treatment is still required after 30 days from the beginning of treatment. One of ordinary skill in the art would reasonably have expected success in administering the therapy for more than 30 days because McDonald discloses that no side effects were noticed in patients administered beclomethasone dipropionate, and furthermore because Bertz et al. discloses that patients maintained on a similar topically active corticosteroid, budesonide, showed no side effects when maintained on the drug for up to 70 days. In view of these disclosures, one of ordinary skill in the art would have determined that beclomathasone dipropionate or budesonide could reasonably be administered for a duration of over 30 days due to the observed lack of side effects for topically active corticosteroids. Moreover, determination of the time period of administration is considered well within the skill of the artisan, involving merely routine skill in the art.

Thus the invention as a whole is *prima facie* obvious over the prior art.

Response to Argument:

Applicant's arguments and declaration submitted March 23, 2007 as applied to the above rejection have been fully considered and not been found persuasive to remove the above rejection.

Applicant argues that at the time of the invention, there were considerable risks to long-term glucocorticoid administration, and that no one skilled in the art would

consider continuing treatment beyond 30 days. Furthermore, Applicant cites the reference Malo et al. to indicate the risks of beclomathasone administration.

However, the disclosure of McDonald et al. specifically overcomes this teaching of the prior art by presenting a course of therapy which is sufficiently well tolerated that it could be extended beyond 28 days. McDonald specifically states that the treatment was well-tolerated, and that typical side effects of corticosteroids, such as microbial infections, hypercortisolism, and adrenal insufficiency, were not observed during the treatment. (p. 32, left column, first paragraph, under the heading, "Toxicity from Treatment," and p. 33, left column, last paragraph – right column, first paragraph) In other words, the treatment was finally stopped because of the study design rather than because the patients could not tolerate further treatment. Therefore, given the demonstrated absence of typical corticosteroid-associated side effects from this therapy, one of ordinary skill in the art would have been motivated to extend the duration of treatment beyond the thirty day treatment disclosed by Macdonald et al., and would have reasonably expected success in doing so, in view of the discovery by McDonald et al. that oral beclomethasone dipropionate does not produce the expected side effects of corticosteroids, such as severe infections. The fact that Applicant himself did not continue the therapy beyond 29 days does not change the fact that other persons of ordinary skill in the art would have interpreted these results as indicating that therapy could in fact be administered for longer durations without the side effects known to exist for systemically administered corticosteroids. While this treatment would require that patients be monitored closely for the appearance of side effects, such monitoring is

well within the ordinary level of skill in the art and is to be expected whenever a patient is being treated with corticosteroids for any length of time.

Furthermore, Bertz et al. discloses that a different topically active corticosteroid, busedonide, produces no side effects even in patients treated for up to 70 days. The teaching of Bertz et al. indicates that at the time of the invention, one of ordinary skill in the art would reasonably consider administering an oral, topically active corticosteroid such as busedonide, for well beyond 30 days. Although the individual durations of therapy for the patients of Bertz et al. ranged between 6 and 70 days, this merely indicates that various durations, of either above or below 30 days, can be used in this therapeutic method. In other words, one of ordinary skill in the art would have administered a topically active corticosteroid for longer than 30 days when the patient's condition warranted such therapy.

With regard to Applicant's citation of Malo et al. to demonstrate the known side effects of beclomethasone dipropionate, the reference concerns administration by inhalation, rather than by oral administration. When weighed against the lack of side effects reported by McDonald et al. and Bertz et al., one of ordinary skill in the art would conclude that oral administration of topically active corticosteroids does not produce side effects of the same severity as administration by inhalation.

Thus Applicant's arguments are not found to be convincing and the rejection is maintained.

Claims 1-10 and 12-18 are rejected under 35 USC 103(a) as being unpatentable over Baehr et. al. (Reference of record in previous office action) in view of Bertz et al. (Reference included with PTO-892)

Baehr et. al. teaches that oral administration of the particular topically active corticosteroid, beclomethasone dipropionate, alone in the form of a capsule for 28 days, is a useful method of treating graft-versus-host disease in a human following organ allograft transplantation of human leukocyte antigen mismatched marrow. (p. 1233, right column, under the heading, *clinical efficacy*) Baehr et. al. also teaches that, in subjects already taking prednisone, "The prednisone dose at study entry was maintained throughout the study whenever medically possible," (p. 1232. left column, 3rd paragraph) meaning that BDP was administered in conjunction with another prophylactic agent as taught by instant claim 16. Baehr et. al. also teach the use of BDP in subjects who have tissue damage of the intestinal mucosa and liver. Baehr et. al. also teaches the effective amount of beclomethasone dipropionate to be 8 capsules of 1 mg each per day, for a total dose of 8 mg per day, in accordance with instant claim 2. (p. 1232, under the heading, *formulation and dosing of beclomethasone dipropionate*) Although adrenal axis function was reduced in patents receiving BDP, no clinical side effects were observed. (p. 1234, right column, p. 1236, right column, second paragraph) Baehr et. al. also suggest that the purpose of the study is to evaluate whether the oral BDP is a safe effective treatment for the instant disease. See the abstract of Baehr et. al. Baehr et. al. does not explicitly disclose the long-term therapy (i.e. 29-56 days) of the claimed invention.

Bertz et al. discloses a method of treating graft-versus-host disease by administering oral budesonide as a topically active corticosteroid. (p. 1186, left column, second paragraph - right column, third paragraph) The duration of the therapy was between 6-70 days, varying from patient to patient, with no side effects observed in any patient. (p. 1187, right column, first paragraph)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to orally administer BDP or Budesonide alone or with prednisone over the long term (i.e. 29-56 days).

One having ordinary skill in the art at the time of the invention would have been motivated to orally administer BDP or budesonide alone or with prednisone in the long term (i.e. 29-56 days) since the administration of BDP alone or with prednisone for 30 days or les is known according to the prior art, and a subject may not have fully recovered from their condition after 30 days, and further because Bertz et al. discloses that budesonide can also be administered for the treatment of graft-versus-host disease. Thus, one of ordinary skill in the art would reasonably extend the therapy to the longer period from 30 days or less to 56 days if such treatment is still required after 30 days from the beginning of treatment. Furthermore because Bertz et al. discloses that patients maintained on a similar topically active corticosteroid, budesonide, showed no side effects when maintained on the drug for up to 70 days. In view of these disclosures, one of ordinary skill in the art would have determined that beclomathasone dipropionate or budesonide could reasonably be administered for a duration of over 30 days due to the observed lack of side effects for topically active corticosteroids.

Moreover, determination of the time period of administration is considered well within the skill of the artisan, involving merely routine skill in the art.

Thus the invention as a whole is *prima facie* obvious over the prior art.

Response to Argument:

Applicant's arguments and declaration submitted March 23, 2007 as applied to the above rejection have been fully considered and not been found persuasive to remove the above rejection.

Applicant argues that the prior art teaches away from long-term (more than 28 days) administration of corticosteroids because of the well-known side effects due to adrenocortical suppression. However, the disclosure of Baehr et al. specifically overcomes this teaching of the prior art by presenting a course of therapy which is sufficiently well tolerated that it could be extended beyond 28 days. Baehr et al. specifically states that, while a decline in cortisol levels was observed in the patients being treated, this decline did not lead to any clinically significant symptoms suggestive of adrenocorticosteroid excess. (p. 1234, right column) No adverse events were observed which could be related to BDP. (p. 1236, left column, last paragraph – right column, first paragraph) In other words, the treatment was finally stopped because of the study design rather than because the patients could not tolerate further treatment. Therefore, given the demonstrated absence of typical corticosteroid-associated side effects from this therapy, one of ordinary skill in the art would have been motivated to extend the duration of treatment beyond the thirty day treatment disclosed by Baehr et al., and would have reasonably expected success in doing so, in view of the discovery

by Baehr et al. that oral beclomethasone dipropionate does not produce the expected side effects of corticosteroids, such as severe infections. While this treatment would require that patients be monitored closely for the appearance of side effects, such monitoring is well within the ordinary level of skill in the art and is to be expected whenever a patient is being treated with corticosteroids for any length of time.

Furthermore, Bertz et al. discloses that a different topically active corticosteroid, busedonide, produces no side effects even in patients treated for up to 70 days. The teaching of Bertz et al. indicates that at the time of the invention, one of ordinary skill in the art would reasonably consider administering an oral, topically active corticosteroid such as busedonide, for well beyond 30 days. Although the individual durations of therapy for the patients of Bertz et al. ranged between 6 and 70 days, this merely indicates that various durations, of either above or below 30 days, can be used in this therapeutic method. In other words, one of ordinary skill in the art would have administered a topically active corticosteroid for longer than 30 days when the patient's condition warranted such therapy.

With regard to Applicant's citation of Malo et al. to demonstrate the known side effects of beclomethasone dipropionate, the reference concerns administration by inhalation, rather than by oral administration. When weighed against the lack of side effects reported by Baehr et al. and Bertz et al., one of ordinary skill in the art would conclude that oral administration of topically active corticosteroids does not produce side effects of the same severity as administration by inhalation.

Thus Applicant's arguments are not found to be convincing and the rejection is maintained.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over McDonald et. al. (References of record in previous office action) or alternately Baehr et. al. (References of record in previous office action), in view of Bertz et al. (Reference included with PTO-892) in view of, alternately, US patents Lundquist, Brancq et. al., or Benita et. al. (US patents 5843465, 5958431, and 6007826, References of record in previous office action).

The disclosures of McDonald et. al. and Baehr et. al. in view of Bertz et al. is discussed above. The above references do not disclose a method in which the active agent is administered as a pharmaceutical emulsion.

Lundquist, Brancq et. al., and Benita et. al. all disclose pharmaceutical emulsions, and methods for preparing the same from hydrophobic pharmaceutical compounds. (see, for example, claim 1 of Lundquist, claim 1 of Brancq et. al., or claim 1 of Benita et. al.)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to orally administer BDP alone or with prednisone as an emulsion, in the manner of claim 11, as disclosed by the aforementioned US patents.

One having ordinary skill in the art at the time of the invention would have been motivated to administer the compound as an emulsion to increase solubility and bioavailability. One of ordinary skill in the art would have reasonably expected success

because determination of the optimal dosage formulation is considered well within the skill of the artisan, involving merely routine skill in the art.

Thus the invention as a whole is *prima facie* obvious over the prior art.

Response to Argument:

Applicant's arguments and declaration submitted March 23, 2007 as applied to the above rejection have been fully considered and not been found persuasive to remove the above rejection. The reasons are the same as those discussed above concerning McDonald et al. and Baehr et al.

Claims 1, 2, 4, 5, 9, 10, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Punch et. al. (Of record in previous office action), in view of Sequeira et. al. (US patent 6057307, of record in previous office action)

Punch et. al. teaches that systemically administered corticosteroids are a standard therapy used to reduce the likelihood of rejection in liver transplant recipients, a therapy which is complicated by the presence of multiple side effects including weight gain, hypertension, hyperlipidemia, glucose intolerance, hirsutism, acne, and osteoporosis. (p. 783, first paragraph) The object of the research disclosed by Punch et. al. was an attempt to relieve said side effects by withdrawing corticosteroid treatment 1 year after transplantation. It should be noted that this reference indicates that corticosteroids can be administered for up to a year in the case of liver transplant recipients, which is well beyond the 30-day point defined by Applicant as marking long-

term therapy. Punch et al. does not disclose topical administration of corticosteroids in order to treat host-versus-graft disease of the liver with reduced side effects.

Sequeira et. al. teaches, "A method of treating a corticosteroid-responsive disease of the lower airway passages or lungs, which comprises administering as initial or maintenance therapy to the surfaces of said lower airway passages or lungs, at least once daily, a substantially non-systemically bioavailable amount of aerosolized particles of mometasone furoate effective for treating said disease." (Claim 1) In other words, the invention of Sequeira et. al. comprises a method of locally treating a disease responsive to corticosteroids by administering mometasone furoate in an inhaleable form locally to the lungs. Sequeira et. al. also teaches that systemically bioavailable corticosteroids cause unwanted side effects (column 1, lines 51-55), and that a major benefit of the claimed invention is that mometasone furoate avoids this complication because it does not become systemically bioavailable from the gastrointestinal tract. (Column 3, lines 40-54) Although Sequeira et. al. does not mention host-versus-graft disease due to lung transplantation by name, this condition falls within the claim language of, "a disease responsive to corticosteroids," which would be treatable by, "a substantially non-systemically bioavailable amount of aerosolized particles of mometasone furoate effective for treating said disease."

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teaching of Punch et. al. by administering an orally available, topically active corticosteroid such as mometasone furoate to the liver, in place of or in addition to standard systemic corticosteroid therapy, by oral administration to a patient

suffering from either graft-versus-host or host-versus-graft disease affecting the intestine and/or liver.

One of ordinary skill in the art would have been motivated to modify the invention in this way in order to treat liver transplant rejection without causing the severe systemic side effects which are observed with existing corticosteroid therapy.

One of ordinary skill in the art would have reasonably expected success because, as taught by Punch et. al. existing corticosteroids were therapeutically effective against liver transplant rejection to the point that they were in common use despite their substantial side effects, and because mometasone furoate was already known, by Sequeira et. al., to be effective at treating corticosteroid-responsive diseases.

Therefore the invention taken as a whole is *prima facie* obvious.

Response to Argument:

Applicant's arguments and declaration submitted March 23, 2007 as applied to the above rejection have been fully considered and not been found persuasive to remove the above rejection. The reasons are the same as those discussed above concerning McDonald et al. and Baehr et al.

Applicant's attention is further drawn to the reference Smith et al., which is made of record in this office action. Smith et al. discloses a study of the glucocorticoid receptor binding and transcriptional activation of a number of topically active glucocorticoids. (p. 957, left column, paragraph 3) Mometasone furoate, fluticasone propionate, triamcinolone acetonide, and budesonide are all disclosed as being topically

active glucucoritcoids that bind to the glucocorticoid receptor and activate transcription. (P. 958, figures 1-3, p. 959, table 1) As all of these compounds are disclosed to be topically active and to activate the same receptor, one of ordinary skill in the art would recognize that mometasone furoate, fluticasone propionate, and triamcinolone acetonide can be substituted fro budesonide in the above-mentioned references.

**Double Patenting**

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-18 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-40 U.S. Patent No. 6096731 (Of record in previous office action, herein referred to as '731). Although the conflicting claims are not identical, they are not patentably distinct from each other because Patent 6096731

is drawn to a method for preventing tissue damage associated with graft-versus-host disease having undergone hematopoietic stem cell transplantation, which is not patentably distinct from the invention claimed by the instant application. The claims of the instant application are drawn to a method of treating a patient requiring long-term therapy following hematopoietic stem cell transplantation having graft-versus-host disease or following organ allograft transplantation having host-versus-graft disease comprising same active agents, with the same claim limitations. A method of "preventing tissue damage" according to claim 1 of '731 is reasonably considered to be a subset of a method of, "treating a patient requiring long-term therapy," according to instant claim 1.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the same active agents in a method of treating a patient requiring long-term therapy following hematopoietic stem cell transplantation having graft-versus-host disease or following organ allograft transplantation having host-versus-graft disease since the same active agents are known to be useful in a method for preventing tissue damage associated with graft-versus-host disease having undergone hematopoietic cell transplantation or intestinal or liver transplantation. With regards to the limitation that the therapy is long-term, the specification of 6096371 provides two examples of the claimed therapeutic method in which therapy is continued for 80 and 90 days, well beyond the point defined in the instant specification as "long-term therapy." (column 6, lines 32-63) Furthermore, claim 11 of '731 states that treatment ceases after 80 days following infusion of hematopoietic cells, indicating an

80 day course of prophylactic treatment, since a prophylactic regimen should be started as soon as possible after transplantation. Therefore, one of ordinary skill in the art at the time of the invention would reasonably have expected that these active agents would have been beneficial in the instant claimed method.

**Summary**

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Eric Olson
Patent Examiner
AU 1623
4/3/07

Anna Jiang
Supervisory Patent Examiner
AU 1623